REMARKS

This amendment with associated comments is filed in response to the most recent Final Office Action in which claims 1, 10-12, and 16-22 were rejected under 35 U.S.C. § 112. Claims 2-9 and 13-15 were previously cancelled. Claim 1 is the only pending independent claim. Claims 1, 10, 11, and 12 have been amended to further clarify steps called for in the claims using words explicitly used in the text of the written description in order to remove any possible doubt or concern about the written description support for the claims and with regard to the enablement of these claims. Applicants sincerely thank the Examiner for withdrawing all rejections on art. We are now down to resolving issues under § 112.

Based on the above amendments and the remarks therein, reconsideration and allowance of all pending claims are requested. No new matter has been added by the amendments, which are fully supported by the specification as originally filed as discussed in detail below. Each of the foregoing rejections is respectfully traversed. Applicants urge the Examiner to favorably reconsider the case and to allow all pending claims.

I. Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1, 10-12, and 16-22 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. While not believed to be well taken, this ground of rejection is rendered moot by reason of the amendments made to the subject claims. Also, as explained below, the claims as amended are also not properly rejectible for any reason under §112, and are now in a position for allowance under all relevant provisions of the Patent Act.

A. Interruption of Fermentation

Possession of a claimed invention may be demonstrated in a variety of ways. *See* M.P.E.P. 2163 (I), page 2100-173, first full paragraph. It is well-settled that "an applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention." *Id.* (citing *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997)). The fact that the claims are not

word for word facsimiles of the text in the written description does not control and is not a sufficient basis for a blanket section 112, first paragraph rejection. The "description need not be *ipsis verbis* [i.e., "in the same words] to be sufficient." *Id.* (citing Martin v. Johnson, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (CCPA 1972)). The fact that an applicant has rephrased in the claims a passage from the specification does not constitute new matter. Accordingly, rewording a specification passage in the claims, where substantially the same meaning remains intact, is permissible. M.P.E.P. § 2163.07 (I). Ultimately, "[i]f a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, ***even if every nuance of the claims is not explicitly described in the specification***, then the adequate description requirement is met." *Id.* at page 2100-180 (citing *Vas-Cath, Inc v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991)) (emphasis added).

Although not required by law, regulation, or otherwise (as is made clear by the legal precedent cited above. and legions of other similar cases), in the interest of advancing prosecution of this case, Applicants have opted to use language directly from the written description to demonstrate beyond question fully adequate §112-compliant support for what is called for in claim 1, as amended, and all claims dependent thereon, in terms of the claim limitation "interrupting." In this regard, after the paragraph defining the term "fermentation" beginning at the bottom of page 6 of Applicants' PCT Publication No. PCT/EP2004/009321 ("Publication"), the text states the following: "Said interruption of the further processing may be accomplished, for example, by maintaining, retaining, keeping, or storing the fermentation harvest broth for at least one hour under appropriate conditions," wherein such conditions are defined later in the document. Applicants maintain that such interruption may therefore consist of embodiments that include "stopping" or "interrupting" the fermentation step before further processing of the fermentation harvest broth. This plainly contemplates many embodiments pertaining to the state of completion of the fermentation process, so long as recombinant polypeptide made by the cell has been secreted into the cell periplasm. Claim 1 as amended herein now derives explicit verbatim specification support under 35 U.S.C. § 112, first paragraph; and the claims are therefore now undisputably compliant with all requirements of §112.

Accordingly, withdrawal of all §112 written description rejections and reconsideration and allowance of claims 1, 10-12, and 16-22 is respectfully requested.

B. Concentrating Fermentation Harvest Broth During Interruption

It is well-settled that, "if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, ***even if every nuance of the claims is not explicitly described in the specification***, then the adequate description requirement is met." M.P.E.P. § 2163.07 (I) at page 2100-180 (citing *Vas-Cath, Inc v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116) (emphasis added). Here, the concentration step would be understood by a person of ordinary skill to refer to embodiments in which the harvest broth is concentrated "before" and/or during the occurrence of the "interruption" step by reason of the explicit and unquestionable support at page 10 of the PCT application. The claims are, however, open. Thus, other steps may be carried out between the duration and occurrence of the fermentation and concentration and/or interruption steps, and the concentration step clearly may, in certain embodiments, blend into or overlap with the interruption step, as may other steps; that is, other specified and/or unspecified steps may blend into or overlap relative to each other, consistent with the open nature of the claims. Reconsideration and allowance of claims 1, 10-12, and 16-22 is respectfully requested.[1]

II. Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1, 10-12, and 16-22 have also been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the information in the disclosure. As mentioned above, the amendments proposed herein are believed to moot this ground for rejection, even though the rejections applied previously are not believed to have been well taken.

A. A Patent Need Not Teach Every Detail

As the Examiner must know, "the test of enablement is whether one reasonably skilled

[1] Even if it is said that a step occurs "after" or "before" another step, this does not mean the steps cannot or may not blend into or overlap with each other, nor that other steps may be interposed between two or more steps blending into or overlapping with each other. Also, the fact that a step may be said or implied to be "after" or "before" another step does not mean the entire step is carried out before or after the other step, nor does it mean that multiple steps could not be occurring simultaneously, in whole or in part.

in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988). As the Examiner must also know, "[a] patent need not teach, and preferably omits, what is well known in the art." *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991).

B. The Examiner Has Not Made Out a *Prima Facie* Case of Unpatentability

The Examiner must make at least a prima facie case that the specification/ disclosure, in combination with what person of ordinary skill in the art would have known at the time of the invention, would lack sufficient information minimally adequate to enable a person of ordinary skill to practice embodiments of the invention without having to engage in "undue" experimentation. With all due respect, no such showing has been made or, even if it had been, the same is obviated by the amendments submitted herein.[2]

The determination that "undue experimentation" would have been required to make and use embodiments of the claimed invention is . . . undertaken by weighing **all** of the so-called "W*ands* Factor." M.P.E.P. § 2164.01(a), Undue Experimentation Factors (emphasis added); citing *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). These *Wands* Factors include the following:

(A)The breadth of the claims;

(B)The nature of the invention;

(C)The state of the prior art;

(D)The level of one of ordinary skill;

(E)The level of predictability in the art;

(F)The amount of direction provided by the inventor;

(G)The existence of working examples; and

(H)The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In the recent Office Action, only factors (A), (C), (E), and (F) were even mentioned. Thus, "all" of the Wands factors were not considered and weighed on the record by the Examiner in

[2] These amendments also clearly obviate the alleged lack of a §112-compliant written description vis-à-vis what is being claimed.

the recent Office Action. Therefore, Applicants respectfully assert that the Office Action fails "on its face" to make a *prima facie* case of unpatentability based on alleged lack of enablement under 35 U.S.C. § 112, first paragraph. This conclusion is explicitly supported by the M.P.E.P. and associated case law as follows:

> It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis **must** consider **all** the evidence related to **each** of these factors, and **any** conclusion of nonenablement **must** be based on the evidence as a whole.

M.P.E.P. § 2164.01(a), Undue Experimentation Factors (citing *Wands*, 858 F.2d at 737, 740, 8 U.S.P.Q.2d at 1404, 1407.). Again, the Examiner has the initial burden in this instance, and Applicants respectfully assert that such burden is not met when the Examiner only discusses and weights a select few of the factors said to favor the Examiner`s position, with no meaningful discussion about others that may not. Applicants therefore contend that the burden remains with the Examiner and has not been discharged. Accordingly, Applicants need not attempt to refute what the Examiner has alleged vis-à-vis lack of enablement. For this reason, reconsideration and allowance of claims 1, 10-12, and 16-22 is respectfully requested or, in the alternative, a more comprehensive assertion by the Examiner including an objective discussion and weighing of **all** of the *Wands* factors relevant to this case should be provided so Applicants can respond to what is alleged to be a prima facie case, assuming one can be made when all factors are fairly considered and weighed.

C. At a Minimum, at least *Wand* Factors (B), (C), and (D) Weigh Fall Heavily in Favor of Applicants.

In determining issues of enablement, "the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985). Applicants can think of few, if any, other areas of technology in which a substantial amount of experimentation would be a more routine and expected activity than in the area to which Applicants' disclosure pertains. Experimentation—

and lots of it—is a standard and expected reality for persons in the field of synthetic protein synthesis using genetically modified bacteria. Thus, with regard to the *Wands* factor regarding "(B) the nature of the invention," such factor weighs sharply in favor of Applicants. The Office Action conveniently makes no assertion relative to this factor.

Once imbued with knowledge of the basic steps and procedures that comprise a novel process for making a recombinant protein according to the steps of the invention claimed in this case, the person of skill is well-equipped with the competence to determine how to practice embodiments of the process in the present case. That is, the person of skill in this art is well-versed in basic technologies for fermenting the growth of prokaryotic cells, including the basic skill set for transformation of such cells with recombinant expression systems as called for in the claims so that the growing prokaryotic cells can be made to cause the secretion of a recombinant polypeptide of interest into the cell periplasm.

While seemingly foreign and exotic technology to ordinary people (even people with significant technical skills in other scientific fields), these matters are basic and fundamental to persons having at least ordinary skill in cellular microbiology involving protein, synthesis, and related fields. From this knowledge possessed by persons of ordinary skill in this art (including the knowledge to know where to go to obtain needed information, etc.) and the knowledge imparted by the detailed description and examples in the instant specification, a person of skill could then relatively easily practice embodiments of the process involving "interruption" of further processing of the fermentation medium.

It has not been shown how, once imbued with a knowledge of this inventive concept, in the context of the claim as a whole, a person of skill in the art would <u>not</u> be able to practice embodiments of the process as claimed without an "undue" amount of experimentation. Again, an "undue" amount of experimentation in this particular art is something more than quite a lot, since the nature of the art steeped in the concept of often having to do hundreds, thousands, or even tens of thousands of experiments to effectuate various embodiments of many inventive concepts, once known.

Additionally, *Wands* factor (C), "the state of the prior art," powerfully favors Applicants because the prior art at the time of the filing of Applicants' disclosure was well-versed in techniques for synthesizing proteins and other biological materials secreted into the

periplasm of genetically modified bacteria. In fact, the ability to make routine measurements during any phase of the steps described in Applicants' disclosure were well within the grasp of a person having ordinary skill in the art. Such steps would include, for example, measuring the conductivity of fluids, measuring the consistency of fluids, centrifugation, and/or filtration, determining secretion of a recombinant protein into the cell periplasm, just to name a few.

What was not known or appreciated at the time of Applicants' invention (as the Examiner acknowledges in the Office Action on page 5, lines 12-14) was that strategic use of an "interruption" of further processing of the fermentation harvest broth, preferably preceded by a "concentrating" step, would translate into higher yields of the desired recombinant protein for recovery from the cell periplasm compared to cell fermentation processes that were completed in the normal manner or in ways taught in the prior art, such as Bochner`s "killing" or "rapid" further processing after full completion of fermentation.

Applicants went against the grain in a patentable manner with their inventive concept of "interrupting" further processing of the fermentation harvest broth once the recombinant polypeptide of interest determined to have been secreted into the cell periplasm. This is unquestionable. And the Examiner cannot lawfully impose a burden on Applicant to explain "how" the claimed process works in the manner claimed without first making an objective showing based on extrinsic evidence that the process as claimed cannot or would not accomplish what the claims say it will. This, the Examiner has failed to do. In this regard, Applicants take issue with the Examiner`s statement in the Office Action on page 7, lines 15-17, that "the mechanism of factors responsible for the increased yield of the recombinant polypeptide in the exemplifications is not fully understood." As the Examiner must know, U.S. patent law has never required a patent applicant to demonstrate knowledge as to why their claimed process works. So long as the Applicants can constructively demonstrate that it does work and show others how to practice embodiments of the process without undue experimentation, the disclosure should be enabling.

There is no requirement that the mechanism underlying an invention or the technical reasons as to "why it works" makes any sense at all or be "understandable." Any curiosity as to why Applicants` invention works merely strengthens the inventiveness and patentability of the same; and is by no means unusual in the practice of patent law. It is "patently"

inappropriate for the Examiner to try to use the fact that the technical reason(s) for the success of the process may be unfathomable or a "mystery" as a basis to challenge enablement, when the specification states and reasonably demonstrates utility and enablement. It is not as though Applicants are claiming a "perpetual motion machine" or some other technical advance which, on its face, would appear technically infeasible or would clearly violate a fundamental law of nature or conflict with established scientific principles. No such claims have been made by Applicants, nor has the Examiner pointed to any.

Applicants teach how to practice the invention, as claimed, and describe preferred conditions, circumstances, and sequences of the interruption step in considerable detail. The fact that it "works" may be a mystery, but Applicants need not demonstrate in the specification an explanation as to the underlying mechanism. In point of fact, the absence of any such requirement (to describe the underlying mechanism as to how/why a process "works") is a fundamental precept of American Patent Law. The Examiner errs by indicating that Applicants must explain why their technology works in order to satisfy enablement under § 112. Nothing has been pointed to which would be reasonably sufficient to raise a doubt about the utility of the claimed process.

It is plainly counterintuitive to think that higher yields of a recombinant polypeptide of interest secreted into a cell's periplasm would be achieved by interrupting further processing of the fermentation broth containing the cell. Conventional wisdom and common sense would teach one to keep the fermentation going as long as possible to achieve maximum yields. Applicants have found this not to be the case, and their specification has not been shown to fail to teach how to practice this inventive concept without "undue" experimentation.

It is evident that the state of the prior art of processing genetically modified bacteria in fermentation processes for the synthesis/ manufacture of recombinant proteins, recoverable from cell periplasm, was generally fairly well advanced and generally fairly well-understood at the time of the invention, and that the requisite knowledge and skill, as asserted above, needed to practice embodiments of the invention, as claimed, is and would have been well within the grasp of a person having ordinary skill in the art.

As indicated above, the level of one of ordinary skill in the art—another *Wands* factor—with respect to this field is relatively high. Of course, the "field" is not the

"invention," as the Office Action suggests. The question is not whether the level of ordinary skill with respect to Applicants' invention is high—the question is whether the level of ordinary skill in the related art of processing genetically modified bacteria for synthesis of a recombinant protein by fermentation is relatively high. With respect, the Office Action confuses these two and impermissibly melds this particular *Wands* factor into a patent-defeating test that would require an applicant to prove (under the guise of demonstrating enablement) that persons having ordinary skill in the art would have already known how to practice Applicants' novel invention. This would turn the Patent Act on its head, and cannot be a reasonable interpretation of what is required under the factors of the In re Wands case.

When a proper view of the level of ordinary skill in the related art as a whole is considered, it becomes clear that such persons would have had all of the tools (and then some) needed to practice embodiments of Applicants' claimed invention with ease as discussed with respect to *Wands* factor (C) above, at the time of applicants' invention, once they learned of the inventive concept described in the claims, in light of what is disclosed in the specification.

Furthermore, Applicants remind the Examiner that the claims are to be amended herein to state the "interruption" step in exact correspondence with wording in the specification exemplifying one or more embodiments of the invention by which interruption of "further processing" of the fermentation medium or "harvest broth" may be accomplished. These plainly contemplate and would have conveyed to a person of ordinary skill an interruption of further processing of the fermentation harvest broth or medium, preferably after or in conjunction with concentration thereof, prior to what the skilled worker would know to be the "completion" of further processing of the broth. Bochner, for example, plainly "completes" fermentation by either killing the cells or "quickly" moving to a next step involving separation of cells from the fermentation broth. Like the other art that preceded Applicants' invention, Bochner shows no thought or hint of any knowledge of the concept of interrupting further processing of the fermentation broth in the manner of a "hold" or other such "interruption" in accordance with embodiments of the presently claimed invention where the harvest broth, which may be concentrated but not treated so as to kill or separate cells from the broth, may be essentially taken "off line" and placed under conditions during the interruption step which Applicants have found can cause an increase in the net yield of the desired recombinant

polypeptide ultimately recovered from the cell periplasm compared to prior fermentation methods where cells were said to have been processed straight away (as taught by Bochner), immediately following what may have been thought to be a fully complete fermentation.

Nothing in the cited art suggests Applicants' unusual and nonobvious inventive "interruption" concept. The specification clearly teaches how to carry out the claimed process steps and what the interruption of further processing may consist of. There should be no great mystery or uncertainty from the specification disclosure of how to do this. Whether persons of skill may understand "why" it works to increase yield has no bearing on whether the process as claimed is enabled, or patentable, and it very plainly is.

III. The Requested Amendments Should Be Entered and Applicants' Arguments Given Full Consideration.

The above-discussed amendments and Applicants' arguments should be entered and fully considered now, rather than requiring Applicants to endure the expense, delay, and effort of an RCE or other further prosecution iterations. Simply amending a claim to correspond exactly to words used in the specification hardly imposes any significant burden on the Examiner, especially given the history of this case and the fact that this should fully resolve all alleged Section § 112 issues in an uncontroversial manner, and would place the claims of this case in condition for allowance.

Also, it is unfair to raise these § 112 issues for the first time in a final office action and then refuse to allow Applicants to show how the Examiner's concerns about the alleged problems can easily be addressed simply by including explicit words from the specification describing known embodiments of the inventive "interruption of further processing" step of Claim 1. The amendments offered herein obviate all remaining grounds for rejection and cannot reasonably be said to be any significant burden on the Examiner, especially since they provide a basis for advancing the case to allowance. Since the prior amendments have overcome all art rejections, Applicants should, in fairness, be able to show how these further amendments overcome any/all possible grounds for the § 112 rejection and make the case ready to issue.

In light of the amendments requested to be entered herein and the associated remarks

set forth above, reconsideration and allowance of all pending claims is once again respectfully requested.

In light of the foregoing, Applicants respectfully request the Examiner reconsider the application, withdraw all prior rejections, and issue a notice of allowance for all pending claims at the earliest possible convenience.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our **Deposit Account No. 12-2355.**

Respectfully submitted,

LUEDEKA, NEELY & GRAHAM, P.C.

By: /Mark S. Graham/

Mark S. Graham
Registration No. 32,355

Date: December 6, 2010
P.O. Box 1871
Knoxville, Tennessee 37901
(865) 546-4305